Atty Dkt 3. 8325-0015 S15-US1 USSN: 09/844,501 PATENT

I. AMENDMENT

In the Claims:

Please cancel claims 1-122 without prejudice and disclaimer and add the following new claims:

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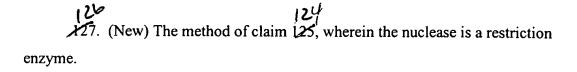
-122. (New) A method for preparing a library of regulatory DNA sequences from a cell, the method comprising:

- (a) providing a cell nucleus, wherein the nucleus comprises cellular chromatin;
- (b) contacting the nucleus with a first enzyme, wherein the first enzyme reacts with accessible regions of cellular chromatin;
 - (c) deproteinizing the cellular chromatin to generate deproteinized DNA;
- (d) contacting the deproteinized DNA with a second enzyme to generate DNA fragments;
- (e) contacting the DNA fragments with a population of vector molecules, wherein the vector molecules comprise a first end that is compatible with the first enzyme and a second end that is compatible with the second enzyme, under conditions favorable to ligation of compatible ends; and
- (f) selecting polynucleotides comprising a DNA fragment ligated to a vector molecule.

124. (New) The method of claim 123, wherein the cell is selected from the group consisting of animal cells, plant cells and microbial cells.

124 125. (New) The method of claim 129, wherein the first enzyme is a nuclease.

25 126. (New) The method of claim 125, wherein the nuclease is DNase I.



127 128. (New) The method of claim 123, wherein the second enzyme is a restriction enzyme.

127 129. (New) The method of claim 128, wherein the restriction enzyme is Sau3A I.

128 130. (New) The method of claim 129, wherein the second end of the vector molecule is generated by digestion with BamH I.

130 131. (New) The method of claim 126, wherein, subsequent to step (b), the DNase I ends are converted to blunt ends.

130 132. (New) The method of claim 131, wherein the first end of the vector molecule is a blunt end.

131 133. (New) The method of claim 132, wherein the first end of the vector molecule is generated by digestion with EcoRV or Smal.

133 134. (New) The method of claim 123 wherein, during steps (b) – (d), the nucleus is embedded in agarose.

134 135. (New) The method of claim 133, wherein a plurality of different libraries of regulatory DNA sequences are prepared, wherein each library is obtained from a different cell.

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135 134 136. (New) The method of claim 135 wherein, in step (a), nuclei are obtained from cells at different stages of development.

134 137. (New) The method of claim 125 wherein, in step (a), nuclei are obtained from cells in different tissues.

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138. (New) The method of claim 135 wherein, in step (a), nuclei are obtained from diseased cells and counterpart normal cells.

135 (New) The method of claim 135 wherein, in step (a), nuclei are obtained from infected cells and counterpart uninfected cells.

139 140. (New) The method of claim 135 wherein, in step (a), nuclei are obtained from cells that express a gene of interest at different levels.

141. (New) The method of claim 123, wherein a plurality of different libraries of regulatory DNA sequences are prepared and, for each library, a different first enzyme is used.

(New) The method of claim 141, wherein the different libraries are combined.

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143. (New) A method for isolating a collection of polynucleotides comprising cellular regulatory sequences, wherein the method comprises:

(a) contacting cellular chromatin with a probe, wherein the probe reacts with accessible regions of cellular chromatin;

- (b) subsequently fragmenting the cellular chromatin to generate a collection of polynucleotide fragments; and
- (c) selectively cloning polynucleotide fragments comprising a site of probe reaction.
- (New) The method of claim 143, wherein reaction of the probe with cellular chromatin results in polynucleotide cleavage at the site of reaction.
- (New) The method of claim 143, wherein the cellular chromatin in present in an isolated nucleus.
- 149 146. (New) The method of claim 145 wherein, in steps (a) and (b), the isolated nucleus is embedded in agarose.
 - 142 147. (New) The method of claim 143, wherein the probe is an enzyme.
 - 146. (New) The method of claim 147, wherein the enzyme is a nuclease.
- 149. (New) The method of claim 148, wherein the nuclease is a restriction enzyme.
 - 1450. (New) The method of claim 148, wherein the nuclease is DNase I.
- 150 151. (New) The method of claim 143 wherein, in step (b), cellular chromatin is fragmented by restriction enzyme digestion.

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150 182. (New) The method of claim 151, wherein the restriction enzyme is Sau3A1.--

Attached is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."